PORTER (W. T.)

Reprinted from the American Journal of Physiology.

Vol. I. — January 3, 1898. — No. I.

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[From the Laboratory of Physiology in the Harvard Medical School.]

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THE earlier experimenters on the coronary arteries described an apparently fundamental difference between the dog's heart and the rabbit's heart.[1] The heart of the rabbit was found to recover easily from fibrillary contractions brought on by the sudden closure of a large coronary artery, by mechanical injury, or by electrical excitation; but the dog's heart never recovered, either spontaneously, or when attempts at assistance were made by massage of the ventricle, stimulation of the ventricle with single induction shocks, or excitation of the vagus. The improbability of so great a difference between the hearts of two nearly related animals has not been able to outweigh the failure of these efforts to revive the dog's heart, and the idea that the heart of the rabbit and the dog are, in this respect, radically unlike, has obtained a wide acceptance.

It is somewhat strange that the belief in the fatal nature of fibrillary contractions in the dog should have become so fixed in the face of MacWilliam's positive statement that recovery can take place. Almost ten years ago MacWilliam,[2] in his refutation of Kronecker and Schmey's[3] hypothesis that fibrillation was caused by the destruction of a coördinating centre located in the interventricular septum near the junction of the upper and middle thirds, wrote as follows: "There is conclusive evidence that all cases of fibrillar contraction of the ventricle cannot be explained by such an hypothesis — the destruction of a coördinating centre localized as indicated above. The fact that recovery may take place — that the ventricles may resume their coördinated rhythm, controverts the idea of the actual destruction of a centre essential for coördination. Such recovery I have witnessed

[1] The literature of this subject is reviewed by W. T. PORTER, Journ. of physiol., 1894, xv, pp. 121–138; and Journ. of exper. med., 1896, i, pp. 46–70.

[2] MACWILLIAM: Journ. of physiol., 1887, viii, pp. 296–310.

[3] KRONECKER and SCHMEY: Sitz.-Ber. der Akad. d. Wiss. zu Berlin, 1884, p. 87.

in several instances in the dog's heart and in a very large number of instances in the hearts of other animals (cat, rabbit, rat, mouse, hedgehog and fowl). Recovery occurs with different degrees of facility in different animals and in different conditions in the same animal. In the dog, recovery occurs with much difficulty and only after the fibrillar contraction has lasted for a considerable space of time; indeed, there very frequently is no recovery apparent — the ventricle may not recommence beating after the incoördinated quivering movement has ceased. At times, however, a number of regular beats are seen after the termination of the fibrillar contraction. . . . In young mammals, fœtal or after birth, recovery appears to be the rule; the fibrillar movement is only a temporary condition, and soon gives place to normal beats" (p. 299).

The neglect of MacWilliam's observations by many subsequent writers is perhaps to be explained by their tacit assumption that fibrillary contractions produced by electrical excitation, — the agent used by MacWilliam for their production, — are not the same as those brought on by mechanical injury or by suddenly cutting off the blood-supply, so that recovery from the former does not necessarily prove the possibility of recovery from the latter. The experiments about to be described will show that this assumption has no foundation, and that the heart of the dog recovers from fibrillary contractions produced in any of these ways. It is true that recovery is much more easily obtained in the rabbit than in the dog, but the difference is merely in degree. There is, with regard to recovery from fibrillary contractions, no essential difference between the rabbit's heart and the dog's heart.

In pondering the cause of failure in the many previous attempts to resuscitate the heart, the following considerations became prominent. It is known that the continued coördinated contractions of the mammalian heart are impossible in the absence of a supply of blood to the cardiac muscle. It is also known that fibrillation arising from whatever cause must, by arresting the heart, cut off what has always been considered the only source of blood-supply to the cardiac muscle, namely, the circulation through the coronary arteries. The restoration of the circulation through the coronary arteries would seem, therefore, to be essential to the restoration of continued coördinated contractions; yet restoring the coronary circulation is a means of treatment that has thus far never been tried. The method of attack, then, should be to maintain an artificial circulation of

defibrinated blood through the coronary arteries of the fibrillating heart.[1]

But at this point it was remembered that the rabbit's heart often recovers spontaneously from fibrillation, although the arrest of the ventricle brings the blood-pressure in the aorta so low as to diminish greatly the circulation through the coronary arteries; and Mac-William, as has already been said, saw even the dog heart recover spontaneously. How, it may be asked, can these hearts in which the coronary circulation was so much reduced have recovered without assistance, if the blood supply through the coronary arteries is so important to recovery? An answer to this pertinent question is furnished by two investigations recently made in this Laboratory, the first of which establishes the fact that the quantity of blood necessary for continued coördinated contractions is less than has been supposed, while the second demonstrates that this necessary quantity can be supplied to the ventricular muscle without the aid of the coronary arteries.

In the first[2] of these investigations the intraventricular pressure and the volume of the coronary circulation in the isolated heart of the cat were recorded simultaneously. It was found that the left ventricle would contract vigorously and for many minutes even when the coronary circulation was reduced to very low limits. The small blood-supply on which a good intraventricular pressure and a regular beat can be kept up is surprising. Reference to figure 1, plate 3 of the Paper in question, will show that admirable contractions were secured with about 3 c.c. per minute. In the experiment of March 13, 1896, fair contractions were seen with a coronary circulation of less than one cubic centimetre per minute; but this heart had been isolated a long time when the observation was made. These experiments are evidence that the mammalian heart will work with a blood-supply hitherto supposed to be wholly insufficient for contractions, even against little or no peripheral resistance.

The second[3] investigation shows this fact still more clearly, and shows beside that blood for continued, coördinated contractions can be obtained without the aid of the coronary arteries. In this research the right ventricle of the excised heart of the cat was kept contracting for several hours with no other blood-supply than that

[1] PORTER: Journ. of exper. med., 1896, i, p. 69.

[2] MAGRATH and KENNEDY: Journ. of exper. med., 1897, ii, pp. 13–34.

[3] PRATT: this Journal, 1898, i, p. 86.

obtained from the interior of the right ventricle through the vessels of Thebesius. The ventricle is tied firmly around a glass tube introduced through the pulmonary artery, the ligature passing below the auriculo-ventricular furrow and closing both veins and arteries. Defibrinated cat's blood is then poured into the tube until the ventricle is full and the blood stands in the tube at a height of one or two inches. The right ventricle will now begin to beat, and, if one of the coronary veins on the surface of the heart is incised, a slight but constant stream of blood will flow from the interior of the ventricle through the foramina Thebesii into the coronary veins and out of the opening on the surface of the ventricle. The blood becomes venous in its course through the heart walls. It has never been seen to enter the coronary arteries. Only that ventricle into which the blood is introduced has been observed to beat; the other ventricle remains inactive. Ringer's solution fails to maintain contractions. A ventricle that has fibrillated violently on the excision of the heart will often resume its coördinated contractions when a circulation is established in this manner through the vessels of Thebesius. Thus the nutrition of the mammalian heart may be maintained in a degree sufficient for long-continued, rhythmic contractions, while the coronary arteries are empty.

It should be observed that the state of the ventricle during fibrillation favors this mode of nutrition. Measurements taken in the left ventricle show that the intracardiac pressure rises at this time.[1] The heart becomes greatly distended. Meanwhile, the pressure in the aorta has fallen very low, the ventricle having ceased to beat, and, in consequence, the pressure in the coronary vessels is also very low. Hence the passage of the blood through the vessels of Thebesius into the coronary veins is doubly aided: on the one hand, by the relatively high pressure in the ventricle; on the other, by the diminished resistance in the coronary vessels. In the excised heart of the cat, an intraventricular pressure of two inches of blood will drive a constant stream through the vessels of Thebesius into the coronary veins, as has been already demonstrated, and the intraventricular pressure during fibrillation is probably greater than two inches of blood.

It should be noted further that the peripheral resistance against which the ventricle must work as it recovers from fibrillation is almost nothing, the arterial pressure having been enormously reduced

[1] PORTER: Journ. of physiol., 1894, xv, p. 132.

by the arrest of the ventricle. Thus the heart just recovering from fibrillary contractions and the heart removed from the body are very much alike in respect to the resistance against which the ventricle works. A difference in this resistance cannot, therefore, be urged against the conclusion that the blood-supply which keeps the isolated heart in rhythmic contraction will support the recovering ventricle until it can re-establish the circulation through the coronary arteries.

This same investigation has revealed yet another way in which the heart muscle may be nourished without the aid of the coronary arteries. On June 26, 1897, a cannula was tied into the distal end of the coronary sinus of the freshly extirpated heart of a cat, and filled with defibrinated cat's blood to a height of about 12 cm. Coördinated, regular, and complete contractions then began. The blood flowed from the coronary veins through the fine connecting vessels into the vessels of Thebesius and thence into the cavities of the heart, changing during its passage from arterial to venous. No blood was observed to enter the arteries. The contractions were facilitated by renewing the blood in the cannula from time to time. After twenty-five minutes the heart fell into pronounced fibrillation. Five minutes later the coördinated contractions were resumed, and continued with occasional pauses during almost half an hour. Again interrupted by fibrillation, they again returned, and both fibrillation and recovery were recorded graphically by a writing-lever attached to the apex. After several such attacks and recoveries the heart became exhausted and would beat no more.

The distension of the right auricle during fibrillation is even more favorable to the nutrition of the heart through the coronary sinus than is the distention of the ventricles and auricles to the nutrition through the vessels of Thebesius, for the coronary sinus is large and its valves are weak, falling back before the pressure of a few inches of blood and opening thus an ample way to vascular areas that may not, indeed, be truly capillary, but are none the less composed of vessels thin-walled enough to permit of nutrient osmosis; else why should the extirpated heart beat for hours when fed in this manner, and why should the blood that enters this path arterial red emerge a venous blue?

It is therefore a mistake to suppose that the feeding of the heart muscle is wholly interrupted by the failure of the circulation in the coronary arteries during fibrillation of the ventricle. A significant

supply is still possible. Usually this endocardiac nutrition, if I may term it so, falls below the required amount, and fibrillation continues to the end. In some instances, however, the endocardiac nutrition is sufficient, and the coördinated beat returns. But these unassisted recoveries are very rare, and all that we at present know seems to point to the advantage of liberally supplying the distracted muscle with defibrinated blood.

An artificial circulation of defibrinated blood through the coronary arteries of the fibrillating dog's heart was therefore established. My method of experiment was as follows: The animals were fully anæsthetized with morphia and ether, tracheotomized, the heart and blood vessels exposed by the resection of the first five ribs on the left, and the first three ribs on the right side, and a cannula placed in the left subclavian artery. The innominate artery was then ligated, and running nooses put around the aorta, just distal to the left subclavian artery, and around the ramus descendens and ramus circumflexus of the left coronary artery, near their origin. The cannula in the subclavian artery was connected to a Mariotte's flask of warmed defibrinated sheep or ox blood, placed high enough to give a pressure of 100 mm. Hg. in the aorta. All being in readiness, the nooses around the coronary arteries were drawn tight, until the heart fell into fibrillary contractions. These arteries were then freed, the noose around the aorta drawn tight, the stop-cock between the subclavian artery and the blood flask opened, and a large glass tube hastily tied into the pulmonary artery. The effect of these procedures was to cause the aorta to fill with sheep's blood at a pressure of 100 mm. Hg.; the semilunar valves being thereby tightly closed, and, every outlet but the coronary vessels being also closed, the blood passed through the coronary vessels into the right heart, whence it escaped out of the pulmonary artery into a dish. This blood was then beaten with a glass rod, filtered through glass wool, shaken with air to oxygenate it, and replaced in the Mariotte's flask.

Eight of these experiments were performed,[1] the first on March 7, 1896, and the last on April 23, 1896. The results were interesting, but not decisive. The character of the fibrillation was always modified by the making of the artificial circulation through the walls of the heart. The little contraction waves which cover the actively fibrillating heart were replaced by large undulations. In the experi-

[1] These experiments were done with the assistance of Mr. W. Tileston and Mr. E. DeW. Wales.

ment of March 21, 1896, these large undulatory movements became at times almost regular. On the whole, the impression made was that the ventricles were often on the point of resuming their coördinated contractions, but never altogether did so. Yet it seemed each moment that they would surely beat.

The hope of ultimate success was strengthened by several encouraging observations. The first was the success which attended the effort to restore coördinated contractions to the fibrillating auricle. Thus, in one dog, the heart began to fibrillate at 11.22 A. M.; the defibrinated blood was immediately turned on, and four minutes later the right auricle, which until then had been fibrillating like the rest of the heart, began to beat in an apparently normal fashion. The second encouraging circumstance was that occasionally, though rarely, a part of the ventricle would contract in a perfectly regular manner, while the remainder of the heart was still in hopeless confusion. The part which thus contracted was a small area in the right ventricle near the origin of the pulmonary artery. The third observation was made April 13, 1896. Pronounced fibrillary contractions appeared 215 seconds after the closure of the ramus circumflexus. The defibrinated blood was turned on, and in a short time movements which resembled feeble normal contractions were seen. Fifteen minutes after the beginning of fibrillation, the stop-cock between the blood reservoir and the aorta was turned off, and the supply of blood through the coronary arteries suddenly checked. Violent fibrillary contractions took place when the heart was thus deprived of its blood-supply. On restoring the circulation two minutes afterward, these gave way, and an almost normal beat returned. At the end of five minutes the circulation was again interrupted, and tumultuous fibrillation again appeared, thus showing that the amount of fibrillation was affected by the blood-supply. But notwithstanding these various signs that success was near at hand, no further progress was made at this time, and it was decided to wait until circumstances made it possible to feed the dog's heart with dog's blood.

While the experiments just described were making, other investigations,[1] on the isolated heart of the cat, afforded frequent opportunities to observe the easy recovery which the heart of that animal may make from fibrillation of long duration. When the isolated heart of the cat is fed through the coronary vessels with defibrinated cat's blood, the ventricles usually beat in a fairly normal fashion. Occa-

[1] MAGRATH and KENNEDY: Journ. of exper. med., 1897, ii, p. 14 and p. 30.

sionally, however, strong fibrillation sets in, very fatal to the hopes of the inexperienced operator. But if the experiment is faithfully continued, and the defibrinated blood kept flowing through the coronary vessels, the apparently hopeless ventricle often springs suddenly from its "delirium" into firm, coördinated beats. In one of the experiments published by Magrath and Kennedy, a cat's heart showed marked fibrillary contractions during forty-five minutes and then fell into regular, normal contractions, which continued more than an hour. It was difficult to believe that a disturbance often so transitory in the cat's heart should be always irrevocably fatal in the dog.

The recovery of the dog's ventricle from fibrillary contractions was finally accomplished during the experiments[1] which led to my discovery that any portion of the extirpated dog's heart, even the "ganglion-free apex," will usually resume its coördinated contractions when fed with the dog's own blood at the proper temperature and pressure.

On March 27, 1897, a dog weighing 10 kilogrammes, anæsthetized with morphia and ether, was bled from the left carotid artery, and the blood whipped, strained through glass wool, and diluted with an equal volume of 0.8% normal saline solution. Normal saline of the same strength, made with tap water, and having a temperature of about 36° C., was meanwhile allowed to flow into the right jugular vein. After a short interval the dog was again bled from the carotid artery. The product of these bleedings was mixed and placed in a reservoir at the temperature of the body. The heart was now extirpated, a cannula tied into the ramus descendens of the left coronary artery, the interventricular septum and the auricles completely cut away, and all the ventricle removed except that portion supplied by the descendens itself. The cannula was then connected to the reservoir of warm blood mixture, and the piece of ventricle perfused with the blood at a constant pressure, which to begin with was about 30 mm. Hg., but which was afterwards raised to 90 mm. Hg. The blood entering the cannula was bright arterial red; that emerging by the coronary vein was venous blue. In a few moments the ventricle began to beat with great vigor, shortening about seven millimetres in vertical diameter. An ordinary muscle lever, magnifying eight times, and weighted with 40 grammes, was fastened to a hook thrust through the apex, and recorded curves about 50 mm. in height. The curves showed some irregularity both in force and frequency. The ventricle

[1] PORTER: Journ. of exper. med., 1897, ii, pp. 391–404.

beat more rapidly when surrounded with blood at the temperature of the body than at room temperature, but the character of the contractions remained unchanged. At 1 P. M., after writing curves for one hour, the ventricle was thrown into fibrillary contractions by stroking its surface with the electrodes of a du Bois-Reymond induction coil (tetanic stimulation). Five minutes later good coördinated contractions returned. Forty minutes thereafter the ventricle was thrown a second time into fibrillary contractions, from which it soon recovered. Two and three quarter hours after the ventricle began to beat, the experiment was broken off. The contractions were by this time very feeble, but still unmistakably coördinated.

On March 29, 1897, a similar experiment was made, also on a dog. When the heart was removed from the body and the "apex" excised, the whole heart fell into fibrillary contractions. The right ventricle recovered from these without assistance, giving a few coördinated beats; the apex recovered on being fed with the defibrinated blood from the same dog, through a branch of the descendens. The apex was then thrown into fibrillation by stroking it with the electrodes of a du Bois-Reymond inductorium (hammer in action), but recovered speedily even when very strong currents were used.

The following day the heart of a dog was removed from the chest, and most of the left ventricle and all of the right ventricle and septum, except a fringe near the ramus descendens of the left coronary artery, were cut away. During the cutting of the heart, strong fibrillation appeared. A part of the right ventricle soon recovered spontaneously from this, giving a few fully coördinated beats.

On the afternoon of this day, in another heart, the part of the left ventricle supplied by the ramus descendens was fed through this vessel for nearly an hour without a pause in its ceaseless fibrillation, but finally a brief series of completely coördinated contractions was observed.

April 5, 1897, a still more remarkable recovery was noted. The part of the left ventricle (dog) nearest the apex was removed and fed through its coronary artery. The piece thus extirpated was 10 mm. in length. When good coördinated beats were secured, a powerful induction current was applied, throwing the perfused apex into fibrillation. Recovery took place in a few seconds. The current was at one time so strong as to burn the heart at the electrode points. The apex was now laid on one side in a beaker of blood. After about an hour, the apex was again perfused, and well coördinated,

but feeble contractions secured. Fibrillation was now easily produced with the induction current and continued a long time, but recovery at last took place.

Finally, in two cases, — the only ones in cardiac literature, so far as I am aware, — the dog's right ventricle fibrillated on its removal from the body, and yet, a moment later, unfed and undistended, gave a few coördinated beats. Continued contraction is of course impossible to the ventricle of the dog without a constant supply of nutrient material with which to replenish its rapidly impoverished intramolecular stores.

The experiments thus far related show that the cat's heart recovers readily from fibrillary contractions when the cardiac muscle is fed with the cat's own blood, and that various portions of the dog's heart, — for example, the auricle, the ventricle, and large parts removed from the ventricle, — will recover if fed with dog's blood; and they bring two cases of unassisted recovery, in which the dog's right ventricle, thrown into fibrillation by the extirpation of the heart, gave spontaneously, without perfusion of its coronary vessels, a few regular, coördinated contractions. They do not include any instance in which the whole dog's heart was recovered from fibrillation; but this is not to be wondered at, for the experiments in which the recovery of the whole heart was attempted were made with sheep or ox blood brought from the slaughter-house, and it is well known that such blood is injurious to the heart of the dog. I hesitated some time before attempting the recovery of the whole heart by the perfusion of dog's blood, for it was certain that two dogs would have to be used for each experiment in order to get sufficient blood for the satisfactory perfusion of the entire heart, and it was possible that many animals would be sacrificed to technical difficulties before a successful result could be reached. Moreover, additional experiments seemed unnecessary, for if the auricle and ventricle recover when separated, they should recover when left in their normal connection. This reluctance was strengthened by two preliminary trials, in each of which the whole dog's heart was fed with dog's blood, but without avail, owing to slight imperfections in method. It was therefore resolved to stop the fibrillation, if possible, before attempting to feed the heart muscle, in the hope that coördinated contractions would return if the perfusion was made after every trace of disordered contraction had disappeared. The entire success of this plan is shown by the following experiments.

Experiment Oct. 25, 1897. A large dog, anæsthetized with morphia and ether, was bled, perfused with 0.8 per cent sodium chloride solution, bled again, and the blood defibrinated and placed in a pressure-flask at the temperature of the body. The heart of a small dog, anæsthetized with morphia and ether, was then exposed, and the venæ cavæ, the right vena azygos, the aorta, and the innominate and left subclavian arteries ligated. Cannulas were placed in the innominate artery, the pulmonary artery, and the two auricles. The cannula in the innominate artery was connected with the pressure-flask, and supplied the coronary arteries with blood, which, after passing through the heart muscle, escaped from the coronary veins and the vessels of Thebesius and found its way out of the heart by the cannulas in the pulmonary artery and auricles. As soon as the warm defibrinated dog's blood was forced through the coronary vessels, the heart, which had ceased to beat while the preparations were making, began to contract in its regular, normal way. Fibrillation of both auricles and ventricles was now induced by stimulating the ventricles and auricles with a rapidly interrupted current from a du Bois-Reymond inductorium. The auricles soon recovered their coördinated contractions, but the ventricles continued to fibrillate for a little more than an hour. The supply of blood to the heart was then cut off, and iced normal saline solution poured upon the heart until every trace of fibrillation had ceased. The coiled bulb of a surface thermometer placed on the ventricle gave a temperature of 22°C. Blood at 36°C. was again allowed to flow through the coronary arteries. The whole heart then began to beat. The contractions were feeble, but entirely regular and fully coördinated.

Experiment, November 3, 1897. The heart of a dog anæsthetized with morphia and ether, was perfused with warm defibrinated dog's blood, as in the preceding experiment. The heart beat very well as soon as the perfusion began. Fibrillation was now brought on by electrical stimulation. The perfusion was then stopped, and iced saline solution poured over the heart until all movement had ceased. On again perfusing the heart with blood at 36°C., thoroughly good contractions, strong, regular, and perfectly coördinated, began. After this strong and regular beating had been watched for some time, fibrillation was again induced, and the heart cooled down, as before. But perfusion was this time recommenced before the last tremor had ceased. The result of this premature action was the return of fibrillary contractions in full force. Twice again the heart was cooled and perfused before fibrillation had wholly ceased, with the same result. Then still another cold bath was given, and this time perfusion was not begun until the ventricle lay quiet. The heart now beat in normal fashion for a long time, the contractions being very forcible and completely coördinated.

Thus the whole dog's heart can be recovered from fibrillary contractions by cooling the ventricles until all trace of fibrillation has disappeared, and then bringing the heart back to the normal temperature by circulating warmed defibrinated blood through the coronary vessels. Doubtless the whole heart of the dog, like the auricles and ventricles, and like the heart of the cat and the rabbit, can also be recovered by persistent feeding with defibrinated blood at normal temperature and pressure, and, in very rare cases, by endocardiac nutrition through the vessels of Thebesius and the coronary veins, but further experiments would only confirm the statements contained in these pages. The thesis with which this Paper began has been sufficiently demonstrated. In respect of recovery from fibrillary contractions, there is no essential difference between the hearts of the rabbit, the cat, and the dog.